



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Eugen Koren and Mirna Koscec

Serial No.: 08/970,045

Group Art Unit:

1645

Filed: November 13, 1997

Examiner:

P. Duffy

For: *ANTIBODIES TO LIPOPROTEINS AND APOLIPOPROTEINS AND METHODS  
OF USE THEREOF*

Assistant Commissioner for Patents  
Washington, D.C. 20231

Feb 08 1999  
GROUP 180

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including eight (8) pages of Form PTO-1449. Most of the documents cited below were cited by or submitted to the Patent Office in Application Serial No. 08/268,809, filed June 30, 1994, to which the present application claims priority. Pursuant to 37 C.F.R. §1.98(d), Applicants are not enclosing copies of these publications. Copies will be provided upon request, however.

Enclosed is a check for \$240.00 representing the fee required under 37 C.F.R. §1.17(p) for an Information Disclosure Statement filed after a first office action on the merits under 37 C.F.R. §1.97(c). It is believed that no additional fees are required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any fees to Deposit Account No. 01-2507.

02/05/1999 RSEGAYE 00000066 08970045

240.00 01 FC:126

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

U.S. Patents

<u>Number</u>	<u>Issue Date</u>	<u>Patentee</u>	<u>Class/Subclass</u>
4,786,589	12/22/88	Pounds et al.	435/005
4,376,110	3/8/83	David et al.	436/513

Foreign Documents

<u>Number</u>	<u>Publication Date</u>	<u>Country</u>
0 407 035 A2	01/09/91	Europe
0 257 778 A2	03/02/88	Europe
WO 86/05493	09/25/86	PCT
WO 93/07165	04/15/93	PCT
WO 93/18067	9/16/93	PCT

Publications

Alaupovic, P., et al., "Characterization of Potentially Atherogenic Triglyceride-rich Lipoprotein Particles", *Klin Wochenschr*, 68:38-42 ( 1990).

Alaupovic, P., et al., "Distribution of Lipoprotein Families in Major Density Classes of Normal Human Plasma Lipoproteins", *Biochim. Biophys. Acta*, 260:689-707 (1972).

Alaupovic, P., et al., "Isolation and Characterization of an apoA-II-Containing Lipoprotein (LP-A-II:B Complex) from Plasma Very Low Density Lipoproteins of Patients with Tangier Disease and Type V Hyperlipoproteinemia", *J. Lipid Res.*, 32:9-19 (1991).

Alaupovic, P., "David Rubinstein Memorial Lecture: The Biochemical and Clinical Significance of the Interrelationship Between Very Low Density and High Density Lipoproteins", *Can. J. Biochem.*, 59:565-579 (1981).

Arntzenius, A.C., "Regression of Atherosclerosis - Benefit can be Expected from Low LDL-C and High HDL-C Levels", *Acta. Cardiol.*, 46:431-438 (1991).

Assmann, G., et al., "The Hypertriglyceridemias: Risk and Management", *Am. J. Cardiol.*, 68(3):1A-4A (1991).

Atmeh, R.F., et al., "Subpopulations of Apolipoprotein A-I in Human High-Density Lipoproteins, Their Metabolic Properties and Response to Drug Therapy", *Biochim. Biophys. Acta*, 751:175-188 (1983).

Avogardo, P., et al., "Are Apolipoproteins Better Discriminators than Lipids for Atherosclerosis?", *Lancet*, 1:901-903 (1979).

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Barth, J.D., et al., "Progression and Regression of Atherosclerosis, What Roles for LDL-Cholesterol and HDL-Cholesterol: A Perspective", *Eur. Heart J.*, 12:952-957 (1991).

Blankenhorn, D.H., et al., "Prediction of Angiographic Change in Native Human Coronary Arteries and Aortocoronary Bypass Grafts", *Circulation*, 81(2):479-476 (1990).

Cardin, A.D., et al., "Degradation of Apolipoprotein B-100 of Human Plasma Low Density Lipoproteins by Tissue and Plasma Kallikreins", *J. Biol. Chem.*, 259(13):8522-8528 (1984).

Clackson, T. et al., *Nature*, 352: 624-628 (1991)

Curry, M.D., et al., "Determination of Apolipoprotein A and Its Constitutive A-I and A-II Polypeptides by Separate Electroimmunoassays", *Clin. Chem.*, 22(3):315-322 (1976).

Curry, M.D., et al., "Electroimmunoassay, Radioimmunoassay, and Radial Immunodiffusion Assay Evaluated for Quantification of Human Apolipoprotein B", *Clin. Chem.*, 24(2):280-286 (1978).

Curry, M.D., et al., "Determination of Human Apolipoprotein E by Electroimmunoassay", *Biochim. Biophys. Acta*, 439:413-425 (1976).

Curry, M.D., et al., "Quantitative Determination of Human Apolipoprotein C-III by Electroimmunoassay", *Biochim. Biophys. Acta*, 617:503-513 (1980).

Cwirla, S.E. et al., *Proc. Natl. Acad. Sci. USA*, 87: 6378-6382 (1990)

Friedewald, W.T., et al., "Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge", *Clin. Chem.*, 18(6):499-502 (1972).

Fruchart, J.E., et al., "Apolipoprotein A-Containing Lipoprotein Particles: Physiological Role, Quantification, and Clinical Significance", *Clin. Chem.*, 38(6):793-797 (1992).

Fruchart et al., *Clin. Chem.*, 28(1):59-62, (1982).

Galeano, N.F., et al., *J. Biol. Chem.*, "Apoprotein B Structure and Receptor Recognition of Triglyceride-rich Low Density Lipoprotein (LDL) is Modified in Small LDL but Not in Triglyceride-rich LDL of Normal Size", 269(1):511-519 (1994).

Galeano, N.F. et al., *J. Biol. Chem.*, 269:511-519 (1994)

Galfré, G., et al., "Preparation of Monoclonal Antibodies: Strategies and Procedures", *Methods Enzymol.*, 73:3-46 (1981).

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Glenner, G.G., "Formazans and Tetrazolium Salts", *In: H.J. Conn's Biological Stains*, The Williams and Wilkins Company, USA, 225-235 (1990).

Goding, "monoclonal Antibodies: Principles and Practice", Academic Press, Inc, New Yorkpp 56-97 (1983).

Gohlke, H., "Influence of the LDS-/HDL-Cholesterol Ratio on Progression and Regression of Atherosclerotic Lesions. A Review of Controlled Angiographic Intervention Trials", *Wien Klin. Wochenschr.*, 104(11):309-313 (1992).

Gordon, T., et al., "High Density Lipoprotein as a Protective Factor Against Coronary Heart Disease", *Am. J. Med.*, 62:707-714 (1977).

Harduin, P., et al., "Modulation of the Expression of Human LDL-Apo B-100 Epitopes by Lipids and Apolipoproteins", *Arterioscl. Thromb.*, 13(4):529-535 (1993).

Hollinger, P., et al., "'Diabodies': Small bivalent and Bispecific Antibody Fragments", *Proc. Natl. Acad. Sci. USA*, 90:6444-6448 (1993).

Hoogenboom, H.R., et al., "Multi-Subunit Proteins on the Surface of Filamentous Phage: Methodologies for Displaying Antibody (Fab) Heavy and Light Chains", *Nucl. Acids Res.*, 19(15):4133-4137 (1991).

Ito, W., et al., "Development of an Artificial Antibody System with Multiple Valency Using an Fv Fragment Fused to a Fragment of Protein A", *J. Biol. Chem.*, 268(27):20668-20675 (1993).

Kane, J.P., "Characterization of Apolipoprotein B-Containing Lipoproteins", *Method. Enzymol.*, 129:123-129 (1986).

Kashyap, M.L., et al., "Radioimmunoassay of Human Apolipoprotein CII - A Study in Normal and Hypertriglyceridemic Subjects", *J. Clin. Invest.*, 60:171-180 (1977).

Keidar, S., et al., "A High Carbohydrate-Fat Free Diet Alters the Proportion of Heparin-Bound VLDL in Plasma and the Expression of VLDL-ApoB-100 Epitopes", *Metabolism*, 39(3):281-288 (1990).

Koren, E., et al., "Isolation and Characterization of Simple and Complex Lipoproteins Containing Apolipoprotein F from Human Plasma", *Biochemistry*, 21:5347-5351 (1982).

Koren, E., et al., "Apolipoprotein A-I and Apolipoprotein B Containing Lipoprotein Particles in Coronary Patients Treated with Extracorporeal Low Density Lipoprotein Precipitation (HELP)", *Atherosclerosis*, 95:157-170 (1992).

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Koren, E., et al., "Characterization of a Monoclonal Antibody that Binds Equally to All Apolipoprotein and Lipoprotein Forms of Human Plasma Apolipoprotein B. I. Specificity and Binding Studies", *Biochim. Biophys. Acta*, 876:91-100 (1986).

Koren, E., et al., "Characterization of a Monoclonal Antibody that Binds Equally to All Apolipoprotein and Lipoprotein Forms of Human Plasma Apolipoprotein B. II. Isolation of Apolipoprotein B-Containing Lipoproteins from Human Plasma", *Biochim. Biophys. Acta*, 876:101-107 (1986).

Koren, E., et al., "Use of 'Pan' Monoclonal Antibody for Quantification of Apolipoprotein A-II", *Arteriosclerosis*, 6:521a (1986).

Koren, E., et al., "Quantification of Two Different Types of Apolipoprotein A-I Containing Lipoprotein Particles in Plasma by Enzyme-Linked Differential-Antibody Immunosorbent Assay", *Clin. Chem.*, 33(1):38-43 (1987).

Krauss, R.M., "Relationship of Intermediate and Low-Density Lipoprotein Subspecies to Risk of Coronary Artery Disease", *Am. Heart J.*, 113(2):578-582 (1987).

Krodel, E., et al., "Technical Challenges in the Development of the CIBA Corning ACS:180 Benchtop Immunoassay Analyzer", *In: Bioluminescence and Chemiluminescence: Current Status*. John Wiley and Sons Inc., New York, 107-110 (1991).

Kuyl, J.M., et al., "Observed Relationship Between Ratios HDL-Cholesterol/Total Cholesterol and Apolipoprotein A1/Apolipoprotein B", *Clin. Biochem.*, 25:313-316 (1992).

Kwiterovich, P.O., Jr., et al., "Prevalence of Hyperapobetalipoproteinemia and Other Lipoprotein Phenotypes in Men (Aged  $\leq$ 50 Years) and Women ( $\leq$ 60 Years) With Coronary Artery Diseases", *Am. J. Cardiol.*, 71:631-639 (1993).

Kwiterovich, P.O., Jr., et al., "Comparison of the Plasma Levels of Apolipoprotein B and A-1, and Other Risk Factors in Men and Women with Premature Coronary Artery Disease", *Am. J. Cardiol.*, 69:1015-1021 (1992).

La Belle, M., et al., "Increased Immunoreactivity of Apolipoprotein B Epitopes During Prolonged Storage of Low Density Lipoproteins", *Clin. Chim. Acta*, 191: 153-160 (1990).

Lee, D.M., et al., "Properties of Apolipoprotein B in Urea and in Aqueous Buffers - The Use of Glutathione and Nitrogen in its Solubilization", *Biochim. Biophys. Acta*, 666:133-146 (1981).

Lopes-Virella, M.F., et al., "Cholesterol Determination in High-Density Lipoproteins Separated by Three Different Methods", *Clin. Chem.*, 23:(5):882-884 (1977).

Lowman et al., *Biochemistry*, 30:10832-10838.

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Maciejko, J.J., et al., "Apolipoprotein A-I as a Marker of Angiographically Assessed Coronary-Artery Disease", *N. Engl. J. Med.*, 309(7):385-389 (1983).

Marcel et al., *J. Lipid Res.*, 28(7): 768-77 (1987).

McGill, D.A., et al., "Relationship of Blood Cholesterol and Apoprotein B Levels to Angiographically Defined Coronary Artery Disease in Young Males", *Coron. Artery Dis.*, 4(3):261-270 (1993).

Mézes. P., "Construction and Biodistribution Studies of Multivalent Single-Chain Antibodies", *Construction and Biodistribution Studies of Multivalent Single-Chain Antibodies, The Fourth Annual IBC International Conference on Antibody Engineering*, December 1993, Coronado, CA.

Miller, N.E., et al., "High-Density Lipoprotein and Coronary Heart-Disease: A Prospective Case-Control Study", *Lancet*, 1:965-968 (1977).

Miller, G.J., et al., "Plasma-High-Density-Lipoprotein Concentration and Development of Ischaemic Heart-Disease", *Lancet*, 1:16-19 (1975).

Milne, R., et al., "The Use of Monoclonal Antibodies to Localize the Low Density Lipoprotein Receptor-Binding Domain of Apolipoprotein B", *J. Biol. Chem.*, 264(33):19754-19760 (1989).

Mulder, K., et al., "An Evaluation of Three Commercial Methods for the Determination of LDL-Cholesterol", *Clin. Chim. Acta*, 143:29-35 (1984).

Olofsson, S-O, et al., "Isolation and Partial Characterization of a Polypeptide Belonging to Apolipoprotein B from Low-Density Lipoproteins of Human Plasma", *Biochemistry*, 19:1059-1064 (1980).

Ortolá, J., et al., "Biological Variation Data Applied to the Selection of Serum Lipid Ratios used as Risk Markers of Coronary heart Disease", *Clin. Chem.*, 38(1):56-59 (1992).

Osborne, J.D., et al., "The Plasma Lipoproteins", *Adv. Prot. Chem.*, 31:253-337 (1977).

Parham, P. "Handbook of Experimental Immunology, Vol. 1: Immunochemistry," Weir, D.M., Editor, Blackwell Scientific Publicatuons, Oxford (1986).

Parmley, S.F., et al., "Filamentous Fusion Phage Cloning Vectors for the Study of Epitopes and Design of Vaccines", *Adv. Exp. Med. Biol.*, 251:215-218 (1989).

Puchois, P., et al., "Apolipoprotein A-I Containing Lipoproteins in Coronary Artery Disease", *Atherosclerosis*, 68:35-40 (1987).

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Savage, M.D., et al., "Avidin-Biotin Chemistry: A Handbook," Pierce Chemical Company, Rockford, IL (1992).

Smith, L.C., et al., "The Plasma Lipoproteins: Structure and Metabolism", *Ann. Rev. Biochem.*, 47:751-777 (1978).

Sniderman, A., et al., "Association of Coronary Atherosclerosis with Hyperapobetalipoproteinemia [Increased Protein but Normal Cholesterol Levels in Human Plasma Low Density ( $\beta$ ) Lipoproteins], *Proc. Natl. Acad. Sci. USA*, 77(1):604-608 (1980).

Socorro, L., et al., "Preparation and Properties of Soluble, Immunoreactive apoLDL", *G.J. Lipid Res.*, 20:631-638 (1979).

Stein, E.A., et al., "Lipids, Lipoproteins, and Apolipoprotein", *In Tietz Textbook of Clinical Chemistry*, W.B. Saunders, Philadelphia, 1002-1093 (1994).

Tornvall, P., et al., "Relation of Plasma Levels and Composition of Apolipoprotein B-Containing Lipoproteins to Angiographically Defined Coronary Artery Disease in Young Patients With Myocardial Infarction", *Circulation*, 88:2180-2189 (1993).

Warnick, G.R., et al., "Dextran Sulfate-Mg<sup>2+</sup> Precipitation Procedure for Quantitation of High-Density-Lipoprotein Cholesterol", *Clin. Chem.*, 28(6):1379-1388 (1982).

Weeks, I., et al., "Two-Site Immunochemiluminometric Assay for Human  $\alpha_1$ -Fetoprotein", *Clin. Chem.*, 29(8): 1480-1483 (1983).

Wollenweber, J., et al., "Comparative Serum Lipoprotein Analysis by Polyacrylamide Disc Gel and Agarose Gel Electrophoresis", *Clin. Chim. Acta*, 29:411-420 (1970).

Wood, P., "Heterogeneous Fluoroimmunoassay", *Principles and Practice of Immunoassay*, Stockton Press, New York, 365-392 (1991).

"Report of the Working Group on Atherosclerosis of the National Heart and Lung and Blood Institute", 2 (Washington, D.C.: Government Printing Office, 1981) DHEW Publication No. (NIH) 82-2035.

"The Lipid Research Clinics Coronary Primary Prevention Trial Results: II, *JAMA*, 251:365-374 (1984).

"Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents", *Pediatrics*, 89:525-584 (1992).

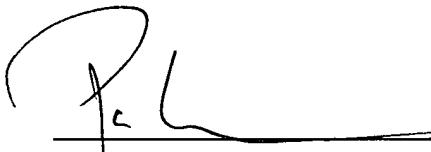
"Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults," *Arch. Intern. Med.* 148:36-69 (1988).

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,



Patrea L. Pabst  
Reg. No. 31,284

Dated: January 29, 1999

ARNALL GOLDEN & GREGORY, LLP  
2800 One Atlantic Center  
1201 W. Peachtree Street  
Atlanta, Georgia 30309-3450  
(404) 873-8794  
(404) 873-8795 (fax)

U.S.S.N. 08/970,045  
Filed November 13, 1997  
Information Disclosure Statement

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: January 29, 1999

  
Kristin Herring